

B
Article 34
c/molt

61
105

CLAIMS

1. Use of an agent that is an agonist of a receptor to which VEGF binds, or a nucleic acid encoding the agonist, for the manufacture of a medicament for the treatment or prevention of intimal hyperplasia of a blood vessel, where the endothelium is wholly or largely intact.
2. Use according to claim 1, wherein the blood vessel is an artery.
3. Use according to claim 1 or claim 2, for the treatment or prevention of stenosis induced by a surgical procedure or associated with pulmonary artery hypertension.
4. Use according to claim 3, wherein the surgical procedure is angioplasty, coronary bypass surgery, surgical anastomosis or endarterectomy.
5. Use according to any preceding claim, for the treatment or prevention of stenosis of the blood vessel.
6. Use according to any preceding claim, for the treatment or prevention of restenosis of the blood vessel.
7. Use according to any preceding claim, wherein the agent is a protein having the function of human VEGF, or a nucleic acid encoding the protein.
8. Use according to claim 7, wherein the protein has the sequence of SEQ. ID No. 2, 4, 6 or 8, or an active fragment thereof.
9. Use according to any of claims 6 to 8, wherein the agent is a nucleic acid in association with a viral or non-viral vector.
10. An implant for therapeutic use, adapted to be placed at or near the site of hyperplasia to be treated or prevented, and containing an agent as defined in any preceding claim.
11. An implant according to claim 10, which is a silastic implant or a biodegradable implant.
12. An implant according to claim 10 or 11, which is in the form of a collar for fitting around a blood vessel at or near the site of the hyperplasia to be treated or prevented.
13. An implant according to any of claims 10 to 12, having an outer wall substantially impermeable to the agent comprised in it.

54
654790-000000

B

62
66Sub
A,
Contd

14. Use of an agent as defined in any of claims 6 to 9, for the manufacture of a medicament for therapy of a condition that can be treated or prevented by stimulation of nitric oxide (NO) and/or prostacyclin production *in vivo*.
15. Use according to claim 14, wherein the condition is hypertension, e.g. essential hypertension, primary pulmonary hypertension or cor pulmonale.
16. A device for use in the delivery of a therapeutic agent to a blood vessel in a patient, which comprises a body adapted to provide a seal around the vessel, the agent being held within or associated with the device so that, in use, the agent comes into contact with the adventitial surface of the vessel.
17. ~~The~~ device according to claim 16, which defines a reservoir between the body wall and the vessel's adventitial surface, the reservoir being at least part-filled by a pharmaceutical formulation containing the agent to be delivered.
18. ~~The~~ device according to claim 17, ~~wherein the~~ ^{wherein said} formulation is in the form of a fluid or gel that is injectable into the reservoir or a paste.
19. ~~The~~ device according to claim 18, wherein the material of the body portion is self-sealing.
20. ~~A device according to any of claims 17 to 19,~~ ^{The device according to claim 17} wherein ~~the~~ ^{said} reservoir can contain up to 10 ml of fluid, preferably at least 2-5 ml.
21. ~~A device according to any of claims 17 to 20,~~ ^{The device according to claim 17, wherein said} wherein the thickness of the body material is generally constant along its length, the reservoir being formed in use by a ballooning of the first body portion between spaced-apart portions that seal against the vessel.
22. ~~A device according to any of claims 17 to 20,~~ ^{The device according to claim 17, wherein said} wherein the thickness of the body material is smaller in an intermediate portion than at spaced-apart sealing portions that seal against the vessel, the reduced thickness forming the reservoir.
23. ~~A device according to any of claims 16 to 22,~~ ^{The device according to claim 16, wherein said} wherein the inner surface of the body comprises a sponge-like material which is capable of being impregnated with a pharmaceutical formulation containing the agent.
24. ~~A device according to any of claims 16 to 22,~~ ^{The device according to claim 16, wherein said} wherein the inner surface of the body is impregnated with a pharmaceutical formulation containing the agent.

00297483 051499

63

87

B

- The device according to claim 16, wherein said*
 25. ~~A device according to any of claims 16 to 24, wherein the material of the body is biodegradable.~~
- The claim*
 26. ~~A device according to claims 25, wherein said material is gelatin, alginate or collagen.~~
- The device according to claim 16, wherein said*
 5 27. ~~A device according to any of claims 16 to 26, wherein the body is moulded or extruded.~~
- The device according to claim 16, wherein said*
 28. ~~A device according to any of claims 16 to 27, wherein the body comprises flexible seal portions that can accommodate expansion of the blood vessel caused by pulsatile blood flow.~~
- The device according to claim 16, wherein said*
 10 29. ~~A device according to any of claims 16 to 28, wherein the body comprises elongate seal portions 8-15 mm long.~~
- The device according to claim 16, wherein said*
 30. ~~A device according to any of claims 16 to 29, wherein the body is generally tubular.~~
- The device according to claim 16, wherein said*
 31. ~~A device according to any of claims 16 to 29, wherein the body has two generally~~
 15 ~~tubular portions which are branched, to form a generally Y- or T-shaped body.~~
- The device according to claim 16, wherein said*
 32. ~~A device according to any one of claims 16 to 29, wherein the body has three generally tubular portions which, at least in use, are branched, to form a generally X-shaped body.~~
- The*
 33. ~~A device according to claim 31 or claim 32, wherein one body portion is generally~~
 20 ~~arcuate in cross-section transverse to its longitudinal extent so as to enable it to surround the exposed portion of a first blood vessel when that vessel is part-embedded in tissue, and longitudinally-extending edges of the first body portion are arranged to be sealed, in use, to the adventitial wall of the first blood vessel or to adjacent tissue.~~
- The device according to claim 16, wherein said*
 34. ~~A device according to any of claims 16 to 33, wherein the body has a longitudinal~~
 25 ~~slit, to facilitate its fitment over the blood vessel.~~
- The device according to claim 16, wherein said*
 35. ~~A device according to any of claims 16 to 34, wherein the body includes an inner layer or helical reinforcement, to increase torsional strength.~~
- claim 1*
 36. A method for delivering an agent as defined in any of claims 1 to 10 to a blood *claim 16*
 vessel, which comprises placing a device according to any of claims 16 to 35 around
 30 the vessel and, if not already present, introducing the agent into the device.

664790 98425260

Add A2